RWLP0032

Journal of Exposure Analysis and Environmental Epidemiology (2000) **10**, 378–384
© 2000 Nature America, Inc. All rights reserved 1053-4245/00/$15.00
www.nature.com/jea

Questionnaire and hair measurement of exposure to tobacco smoke

W.K. AL-DELAIMY,[a] J. CRANE[b] AND A. WOODWARD[a]

[a]*Department of Public Health, Wellington School of Medicine, University of Otago, Wellington, New Zealand*
[b]*Department of Medicine, Wellington School of Medicine, University of Otago, Wellington, New Zealand*

To assess the relation between nicotine and cotinine levels in hair and reported exposure to environmental tobacco smoke (ETS), hair samples from 112 children (aged 3 months to 10 years) and 76 of their mothers were analyzed and information on the smoking habits of household adults in the preceding 6 months recorded. It was found that the levels of nicotine in children's hair were related to the number of smokers in the house, and increased with the total number of cigarettes smoked by all household adults ($P<0.0001$). In a multiple regression analysis, mother's smoking was much more a contributor to children's nicotine levels than smoking by the father or other household adults. Cotinine levels were less strongly associated with reported ETS exposure than nicotine. There was a strong correlation between nicotine hair levels in children and mothers ($r_s=0.7$, $P<0.0001$). However, nicotine levels in the hair of active smokers were not correlated with the reported number of cigarettes they smoked per day. In this population, there was a consistent relation between exposure to ETS (assessed by questionnaire) and dose (as measured by nicotine in hair). We conclude that hair nicotine levels rather than hair cotinine levels provide an informative and objective measure of ETS exposure. The number of cigarettes smoked by active smokers may not be an accurate measure of the total nicotine levels in their bodies. *Journal of Exposure Analysis and Environmental Epidemiology* (2000) **10**, 378–384.

Keywords: *cotinine, hair, nicotine, tobacco smoke pollution.*

Introduction

The risk of environmental tobacco smoke (ETS) to human health has been reported in many studies, ranging from molecular laboratory investigations to large population epidemiological surveys. However, there exists no "gold standard" measure for ETS exposure and lack of an accurate measure may lead to issues of validity and precision of exposure estimate (Jaakkola and Jaakkola, 1997) and misclassification of subjects according to their ETS exposure (Gori, 1994,1995). This has important implications to public health research and policy of the relation between ETS exposure and human health.

Questionnaires are the most widely used method in ETS exposure studies. Although questionnaires are indispensable tools in epidemiological surveys, they lack precision to quantify low levels of ETS exposure (Eliopoulos et al., 1996). In addition, questionnaires are subject to recall and reporting bias. Biomarkers are less liable to these types of error, but may not be sufficiently sensitive to detect very low exposures. Cotinine (a metabolite of nicotine) in body fluids has been used in many studies for the assessment of ETS (Strachan et al., 1989; Benowitz and Jacob, 1993; Crawford et al., 1994; Haddow et al., 1994; Wang et al., 1997), but its short half-life and the metabolic variability in clearance rates among individuals are some of the disadvantages (Coultas et al., 1990; Idle, 1990; Nelson, 1994). Levels of nicotine in hair may be a good alternative indicator for assessment of exposure (Nafstad et al., 1995; Dimich-Ward et al., 1997; Pichini et al., 1997), with the distinct advantage of reflecting long-term exposure. Each centimeter of hair represents more than 1 month of exposure because hair has a uniform growth rate of 1±0.3 cm/month (Uematsu et al., 1995). Furthermore, nicotine stays in the hair shaft for long periods in a stable form without being depleted or degraded (Zahlsen and Nilsen, 1994). Nicotine in hair is believed to be derived from the systemic circulation (Mizuno et al., 1993; Eliopoulos et al., 1996; Pichini et al., 1997), although Nilsen et al. (1994) and Gerstenberg et al. (1995) suggest that nicotine may be adsorbed into hair from the environment.

In human exposure assessment, the aim of any measurement method is to minimize the error in measuring a certain exposure and thereby obtain the most accurate assessment of risks to health. "Exposure" in epidemiology includes any agent relevant to human health that humans are exposed to. "Dose" is the amount that actually crosses the boundary between the environment and the human body (Zatarian et al., 1997). Determining the dose (by the use of biomarkers), rather than simply measuring the presence or absence of exposure in the environment, should reduce measurement error (Armstrong et al., 1992). The aim of this study is to assess the relation of hair nicotine and

1. Address all correspondence to: Dr. W.K. Al-Delaimy, Department of Nutrition, Harvard School of Public Health, Boston, MA 02115.
Received 26 October 1999; accepted 25 May 2000.

Cotinine in hair

PM3006484807

Source: https://www.industrydocuments.ucsf.edu/docs/yzhj0001

cotinine levels (representing measures of dose) to the history of ETS exposure as assessed by the questionnaire.

Materials and methods

A cross-sectional survey of children admitted to Wellington Hospital in winter of 1996 was undertaken. To be eligible for the study, children had to be between 3 months and 10 years of age (to exclude active smokers in older age children), not suffering from debilitating illnesses (e.g., cancer, nutritional disorders) that might alter hair growth velocity, and to have enough hair to be sampled for analysis. In addition, a caregiver (mother, father or other persons taking regular care of the child) had to be available to be interviewed for the study. This selection process was done with the assistance of the nurse in charge of the child. Since this was not intended to be a representative sample, oversampling children from houses that included smokers, by limiting inclusion of children from houses with no smokers, was deliberately done to provide a range of exposures.

After approaching caregivers and obtaining their consent, a questionnaire of the smoking habits of household members (number of cigarettes) was completed, and the average amount of time the child spent away from the home was recorded. Visitors' smoking habits were less accurately recalled by caregivers in terms of the number of cigarettes they smoked and were therefore not included in the multiple regression analysis. Glasgow et al. (1998) and Greenberg et al. (1989) both found that including questions about visitors' smoking habits added no further information to assessment of ETS exposure inside the house.

Hair samples were collected from children and their caregivers. Since very few caregivers' hair samples were from the father and only one was from a grandfather, only the mother's hair samples were included in the analysis. Information on hair dyes, bleaching or other cosmetic treatments was not included in the questionnaire, since the target sample of the study was young children (some mothers may have treated their hair, and such treatments have been found to decrease nicotine levels in hair) (Jurado et al., 1997).

Hair samples from 112 children and 76 mothers were analyzed. An approximated hair sample of 50–100 mg was cut as close as possible to the scalp from the rear part of the head from each individual and stored in paper envelopes at room temperature. The most proximal 1–2 cm of the hair samples were cut and analyzed by radioimmunoassay for nicotine and cotinine by the Division of Clinical Pharmacology and Toxicology at the University of Toronto, Canada (for details of the method, see Klein et al., 1994). All samples were blinded to the analyzing technicians. The sensitivity of this method was 0.1 ng nicotine/mg hair. For cotinine, the sensitivity of the assay was 0.05 ng cotinine/mg hair. For the purpose of statistical analysis, hair samples with "undetectable" levels of nicotine were assumed to have 0.05 ng nicotine/mg hair, and samples with "undetectable" cotinine levels were assumed to have 0.025 ng cotinine/mg. There were 31 (27.7%) children with undetectable nicotine in hair and 42 (37%) with undetectable cotinine in hair.

The study protocol was approved by the Wellington Ethics Committee.

Data Analysis

Nicotine and cotinine results were log-transformed to minimise the skewness of the distributions. The Wilcoxon and Kruskal–Wallis rank sum tests were used to determine the significance of the difference in nicotine and cotinine levels among different exposure groups. The significance of the difference between individual categories of total cigarettes smoked in the house was assessed by the GLM (General Linear Model) procedure in SAS (SAS Inc., Cary, North Carolina) and using the least square means option. Simple linear and multiple regression analyses were used to estimate the exposure–dose relation of nicotine to questionnaire measure of smoking in the house. In analysis involving the total number of cigarettes smoked, two children who were breastfed in the last 3 months were excluded, since there have been reports of increased levels of urine cotinine among children of smoking mothers who were also breastfeeding compared to those not breastfed (Labrecque et al., 1989). Spearman and Pearson correlation coefficients were used for the assessment of the strength of the correlation between nicotine and cotinine levels of children and their mothers. SAS statistical software was used for the above analysis.

Results

Children's Hair Analysis

Nicotine levels in children's hair ranged from undetectable (<0.1 ng/mg hair) to 24.7 ng/mg hair, and cotinine

Table 1. Median, and 25th and 75th percentile hair nicotine levels of a population of hospitalized children in Wellington, New Zealand, in 1996, and the number of children according to the number of smokers in their homes.

Number of smokers in the house	*N*	Median hair nicotine level, ng/mg	Percentiles	
			25th	75th
0	23	Undetectable <0.1	<0.1	0.1
1	48	0.275	<0.1	1.35
2	29	1.46	0.75	2.75
>2	12	2.02	1.08	4.41

PM3006484808

Source: https://www.industrydocuments.ucsf.edu/docs/yzhj0001

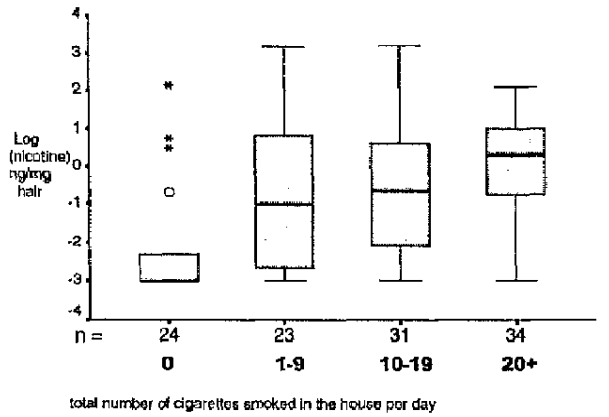

Figure 1. Nicotine hair levels of children hospitalized in Wellington, New Zealand, in 1996, on the logarithmic scale according to the categories of the total number of cigarettes smoked by household adults. Whiskers are the 99% range of values, boxes are 25th–75th percentiles, line across the box is the median. *, Extreme values; O, outliers; *n*, the number of children in each category. Log nicotine ng/mg hair: the logarithm of nicotine levels in nanogram per milligram of hair from the children (0, 1–9, 10–19, 20 +): categories of the total number of cigarettes smoked per day by household adults.

ranged from undetectable (<0.05 ng/mg hair) to 1.5 ng/mg hair. As a simple measure of the relation of children's hair nicotine and cotinine levels with questionnaires, nicotine and cotinine levels in children's hair were related to the number of smokers in the house ($P<0.0001$, Kruskal–Wallis). Table 1 shows that the median nicotine hair levels in children increased with the number of smokers in the house.

On a finer scale, the numbers of cigarettes smoked by individuals in the home were categorized into four (see Figure 1), and these were statistically different in relation to nicotine levels in children's hair ($P<0.0001$, Kruskal–Wallis). These categories were chosen to ensure approximately similar number of children within each group. The differences between individual categories were found to be significant except those between categories "1–9" and "10–19" ($P<0.89$). There was a less significant differentiation of the categories in relation to cotinine in hair of children ($P=0.0058$, Kruskal–Wallis). There was no interaction of age and the time children spent outside their home per week with these categories in relation to nicotine or cotinine in hair.

A statistically significant linear relationship was found between hair nicotine levels in children and the total number of cigarettes smoked by household adults (coefficient estimate (*B*): 0.063, standard error of the mean (SEM): 0.011, $P<0.0001$), but this was less marked for cotinine levels in hair (*B*: 0.019, SEM: 0.007, $P=0.0084$). There was approximately a 6.5% increase in the level of nicotine in children's hair with every cigarette per day smoked in the household. When restricting the analysis to houses that had smokers, the linear relationship was still significant for nicotine (*B*: 0.045, SEM: 0.013, $P=0.0013$) but was not so for cotinine (*B*: 0.013, SEM: 0.008, $P=0.11$).

When questionnaire variables related to ETS at home (number of cigarettes smoked by the mother, father, and all other adults per day) were included in a multiple regression model, they were significantly related to children's hair nicotine ($P<0.0001$), with the mothers' smoking having a stronger effect on these levels than smoking by the father or other household adults (see Table 2 for details). With every cigarette the mother smoked, there was a 10.5% increase in hair nicotine levels of children. Fathers' smoking habits were also related to hair nicotine levels of children, but the effect was less than that of mothers' (there was a 4% increase in hair nicotine levels of children with every cigarette the father smoked). The combined effects of all adults (other than parents) had a

Table 2. Multiple regression values for the relation of log-transformed nicotine and cotinine hair levels to the number of cigarettes smoked by the mother, father and other household adults.

	Regression independent variables			
	Intercept	Mothers' number of cigarettes per day	Fathers' number of cigarettes per day	Other adults' number of cigarettes per day
Nicotine hair levels				
Estimate	−1.747	0.0996	0.0410	0.0493
SEM	0.2175	0.0220	0.0194	0.0211
P value	0.0001	0.0001	0.0364	0.0214
Cotinine hair levels				
Estimate	−2.9349	0.0259	0.0105	0.0203
SEM	0.1356	0.0137	0.0121	0.0132
P value	0.0001	0.0613	0.3846	0.1268

PM3006484809

Source: https://www.industrydocuments.ucsf.edu/docs/yzhj0001

significant effect on the regression equation and there was a 5% increase in hair nicotine levels with each cigarette smoked by adults (other than parents) in the house of the child. Most (77.4%) of the 31 homes with adults who smoked had only one adult smoker.

The same model was not significant for hair cotinine (Table 2), and the relation of the mothers', fathers' and other adults' smoking habits was much weaker.

Mothers' Hair Analysis

For the mothers, nicotine levels in hair varied from undetectable to 70 ng/mg hair, and cotinine levels ranged from undetectable to 5.7 ng/mg hair. There was a significant difference between the levels of nicotine and cotinine in hair of active smoking mothers and non-smoking mothers ($P<0.0001$, Wilcoxon) (see Figure 2).

The number of cigarettes smoked by mothers who were active smokers was neither significantly related to levels of nicotine in their children's hair or their own hair in a simple linear regression model ($P=0.96$, $P=0.52$, respectively). This relation was unchanged when adjusted for the smoking habits of other adults in the home. On the other hand, there was a strong and significant correlation between nicotine levels in hair of children and their mother's hair nicotine levels ($r=0.7$, $P<0.0001$). There was a weaker correlation between cotinine levels in hair of children and maternal hair cotinine levels ($r=0.56$ $P<0.0001$).

Nicotine hair levels were strongly related to cotinine hair levels among mothers' hair samples ($r_s=0.9$, $P<0.0001$) and that of the children ($r_s=0.8$, $P<0.0001$).

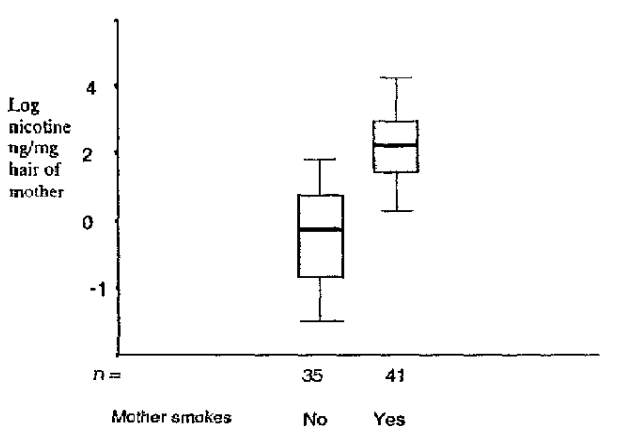

Figure 2. Distribution of nicotine hair levels of mothers of children hospitalized in Wellington, New Zealand, in 1996 according to their smoking habits. Whiskers are the 99% range of values, boxes are 25th–75th percentiles, line across the box is the median. Mother smokes: the mothers' smoking habit; Y: yes, the mother smokes; N: no, the mother does not smoke; *n*, the number of mothers in each category. Log ng nicotine/mg hair: the logarithm of nicotine levels in nanogram per milligram of hair from the mother.

Discussion

Children's Hair Nicotine Levels as a Measure of ETS Exposure

There was a statistically significant positive exposure–dose relation between reported smoking history of all household members (number of cigarettes smoked daily) and levels of nicotine in children's hair. However, there are many other factors which have something to do with smoking that affect ETS exposure assessment using the number of cigarettes. For example, Zahlsen et al. (1996) found in controlled ETS exposure environments that there is a 4–10-fold variation in air nicotine levels for the same number of cigarettes smoked. This variation is also expected for subjects exposed to similar number of cigarettes, which may be due to differences in room ventilation and size, distance from smoking source, number of hours of exposure, and other sources of ETS exposure (Coghlin et al., 1989; Greenberg et al., 1989; U.S. EPA, 1992; Nafstad et al., 1995). This would explain the relatively low (21%) variability in hair nicotine levels of children predicted by the total number of cigarettes smoked at home using the linear regression model.

Mothers' smoking habits were more strongly related to the children's nicotine levels than smoking by the father or smoking by other adults living in the house. This could be explained by the fact that children spend more time around their mothers than with their fathers or with other adults living in the house. Other studies have also reported mothers to be the most important source of ETS exposure to children (Greenberg et al., 1989; Cook et al., 1994; Bono et al., 1996; Knight et al., 1996). Coultas et al. (1987) reported no effect of smoking by the father, while results from this study suggest that there is an association with the dose of ETS absorbed by the children, but this is secondary to the effect of mother's smoking. This has also been found in other studies (Jarvis et al., 1985; Cook and Strachan, 1997). The effect of household adults' (other than the parents') smoking habits on children's hair nicotine levels was important when combined into a composite variable, but had no effect individually. Similarly, the combined number of cigarettes smoked by the mother, the father and other household adults was significantly related to hair nicotine levels of children, but this relation was not seen when the numbers of cigarettes smoked by the mothers, fathers, or household adults were examined separately in simple linear regressions. This suggests that hair nicotine is best regarded as an integrated measure of the dose resulting from multiple ambient sources of ETS in the home.

Mothers' Hair Nicotine Levels as a Measure of Active Smoking

Levels of nicotine in mothers' hair were higher than in children, which was expected since none of the children was

PM3006484810

Source: https://www.industrydocuments.ucsf.edu/docs/yzhj0001

an active smoker while 50% of mothers was. The fact that children's hair nicotine levels and maternal hair nicotine levels were closely correlated suggests that there is a common exposure source among them. Most likely, this source is present at home. For children, most of their exposures to ETS occur in the home environment (Greenberg et al., 1989; Ashley and Ferrence, 1998). For the mother, there could be other sources of exposure from outside the home, which explains the imperfect $(0.7)^2$ value of the coefficient of variation (i.e., 49% of the variability in children's nicotine levels may be predicted from the mothers' nicotine levels).

The correlation between hair nicotine levels of non-smoking mothers and their children's hair nicotine levels was significant ($r=0.57$, $P=0.0004$) while that of smoking mothers and their children was not ($r=0.28$, $P=0.07$). Active smokers receive a much higher dose of nicotine than passive smokers (up to 200-fold higher levels; Hoffmann and Hoffmann, 1987), and there may be much greater variability in uptake of nicotine than that which occurs among passive smokers. Important influences on the uptake of nicotine include the differences in sidestream (SS) and mainstream (MS) particle size and distribution (nicotine, e.g., is in particle phase in MS but in vapour phase in SS) (U.S. EPA, 1992, p. 37).

Differences in smoking habits, such as the type of cigarettes, the depth and rate of smoke–puff pattern of smoking a cigarette, environmental factors affecting combustion of the cigarette, and moisture content of the tobacco (U.S. EPA, 1992, p. 36) may explain the unexpected finding in our study that the number of cigarettes smoked by mothers does not closely correlate with levels of nicotine in their hair. Other investigators have reported a positive relation between number of cigarettes smoked by active smokers and nicotine hair levels ($r=0.48$, $P<0.004$; Eliopoulos et al., 1996; $r=0.69$, $P<0.001$; Mizuno et al., 1993; Dimich-Ward et al., 1997). However, in this current study, recruitment of smokers was by a community survey, and study populations chosen in this manner may be less accurate and consistent in their smoking reports (Wagenknecht et al., 1992) than other groups. Mizuno et al. (1993) and Eliopoulos et al. (1996) recruited volunteers from participants of drug treatment programs and hospital staff. The latter study populations may give smoking histories more accurately. In addition, both studies used controlled conditions and standard protocol experiments, which most probably minimised questionnaire measurement error. The other study by Dimich-Ward et al. (1997) included only five smokers in their study, which may not be enough to show the range and variability of exposure. Furthermore, Nafstad et al. (1997) reported that the personal smoking history of mothers was significantly and well related to their hair nicotine levels (B: 2.7, 95% CI: 1.75–3.55). In their study, they included both smoking (52%) and non-smoking (48%) mothers, which is likely to increase the apparent correlation between the number of cigarettes smoked by mothers and hair nicotine levels. In our study, when we included non-smoking mothers in the analysis, the association between the number of cigarettes per day and hair nicotine levels was, as expected, much increased ($r=0.73$, $P<0.0001$) compared with $r=0.1$, $P=0.5$ when they were excluded.

A previous study by Eliopoulos et al. (1994) included 94 mothers and their infants identified from newborn nurseries in Toronto, Canada, and found no correlation between the number of cigarettes smoked by active smoking mothers and their hair nicotine or cotinine levels. Koren et al. (1992) reached a similar conclusion in their study on a group of mothers and their newborn infants.

Nicotine and Cotinine

Cotinine was present in lesser amounts in hair than nicotine. This has been previously reported from human studies (Kintz et al., 1992; Eliopoulos et al., 1994,1996), and in controlled ETS exposure trials in animals, the difference may be up to 10-fold (Gerstenberg et al., 1995).

The strong correlation between nicotine and its main metabolite (cotinine) in the hair of both adults and children suggests that hair nicotine is mainly derived from the bloodstream rather than adsorbed directly from the environment (Mizuno et al., 1993; Knight et al., 1996). Cotinine is only formed inside the body after metabolism of nicotine, and therefore is unlikely to be strongly correlated to nicotine in hair if a substantial fraction of the nicotine is directly adsorbed from the environment.

The association between cotinine in hair of children and cotinine in mothers' hair was weaker than that for nicotine. It seems that cotinine does not follow the same body distribution as that of nicotine, and it could be that nicotine has better affinity to hair than cotinine. The higher percentage of children with undetectable cotinine in their hair and the lower levels of cotinine in hair, in general, support this argument. Luck and Nau (1984), for example, found that compared to their serum levels, nicotine levels in breastmilk were higher while cotinine levels were lower. There may also be high interindividual variability in the clearance of cotinine (Coultas et al., 1990).

Cotinine in hair of children and mothers was less strongly correlated with reported history of exposure than nicotine. Other investigators reported different results. For example, Eliopoulos et al. (1996) found cotinine in hair to be more strongly correlated to reported tobacco smoke ($r_s=0.57$, $P=0.0008$) than nicotine ($r_s=0.48$, $P=0.004$). However, all the participants in the study by Eliopoulos et al. (1996) were active smokers. When analysis of our subjects was limited to active smoking mothers, hair cotinine was more

PM3006484811

Source: https://www.industrydocuments.ucsf.edu/docs/yzhj0001

strongly related to the number of cigarettes smoked by mother than nicotine, although both were non-significant. This stronger relation of cotinine to the number of cigarettes smoked in active smokers could be explained by the longer half-life in blood (i.e., longer plateau phase), making cotinine less vulnerable to the variation caused by active smoking habits mentioned above over time. Others have found no difference in hair cotinine levels between non-smokers and passive smokers and therefore concluded that only nicotine levels in hair can be used to differentiate smokers, passive smokers and non-smokers (Kintz et al., 1992; Dimich-Ward et al., 1997). On the other hand, the much lower cotinine levels recorded in hair in comparison to those of nicotine mean that cotinine is likely to be much less sensitive as a measure of ETS.

Although we did not control for possible confounding by thickness or color of hair, or rate of growth, it is unlikely that these factors account for much of the variation in the measures of nicotine content in hair. This assumption is based on studies of hair uptake of nicotine under controlled smoke chamber conditions (Jurado et al., 1997), and the consistency of the association with children's hair nicotine levels in our study of different measures of ETS exposure in questionnaires (number of cigarettes, number of smokers) and hair (maternal hair nicotine and cotinine levels).

Conclusion

In this study, nicotine levels in children's hair were related to the number of smokers in the household of the child and the total number of cigarettes smoked in the home. However, among active smokers, we did not observe a relationship between number of cigarettes smoked and hair nicotine levels. Our findings indicate that nicotine in hair is a more sensitive measure of ETS exposure than cotinine in hair. This method of measuring ETS exposure appears to offer some advantages; because of the slow hair growth rate, hair nicotine levels provide an integrated measure of exposure over a period of weeks to months rather than a measure of a point in time, and it is sensitive and specific to tobacco smoke.

Acknowledgments

The study was supported by the University of Otago Research Grant and the Wellington Medical Research Foundation. The authors thank Mr. Gordon Purdie for his statistical input. The authors also thank the Division of Clinical Pharmacology and Toxicology at the University of Toronto, Canada for analyzing the hair samples of the subjects.

References

Armstrong B., White E., and Saracci R. Principles of exposure measurement in epidemiology. Monographs on Epidemiology and Biostatistics, Vol. 21. Oxford University Press, New York, 1992, pp. 236–239.

Ashley M., and Ferrence R. Reducing children's exposure to environmental tobacco smoke in homes: issues and strategies. *Tobacco Control* 1998: 7: 61–65.

Benowitz N.L., and Jacob P. Nicotine and cotinine elimination pharmacokinetics in smokers and non-smokers. *Clin Pharmacol Ther* 1993: 53: 316–323.

Bono R., Russo R., Arossa W., et al. Involuntary exposure to tobacco smoke in adolescents: urinary cotinine and environmental factors. *Arch Environ Health* 1996: 51: 127–131.

Coghlin J., Hammond S.K., and Gann P.H. Development of epidemiologic tools for measuring environmental tobacco smoke exposure. *Am J Epidemiol* 1989: 130: 696–704.

Cook D.G., and Strachan D.P. Health effects of passive smoking: 3. Parental smoking and prevalence of respiratory symptoms and asthma in school age children. *Thorax* 1997: 52 (12): 1081–1094.

Cook D.G., Whincup P.H., Jarvis M.J., et al. Passive exposure to tobacco smoke in children aged 5–7 years: individual, family, and community factors. *BMJ* 1994: 308: 384–389.

Coultas D.B., Howard C.A., Peake G.T., et al. Salivary cotinine levels and involuntary tobacco smoke exposure in children and adults in New Mexico. *Am Rev Respir Dis* 1987: 136: 305–309.

Coultas D., Samet J., McCarthy J., et al. Variability of measures of exposure to environmental tobacco smoke in the home. *Am Rev Respir Dis* 1990: 142: 602–606.

Crawford F.G., Mayer J., Santella R.M., et al. Biomarkers of environmental tobacco smoke in pre-school children and their mothers. *J Natl Cancer Inst* 1994: 86: 1398–1402.

Dimich-Ward H., Gee H., Brauer M., et al. Analysis of nicotine and cotinine in the hair of hospitality workers exposed to environmental tobacco smoke. *J Occup Environ Med* 1997: 39 (10): 946–948.

Eliopoulos C., Klein J., Phan K., et al. Hair concentration of nicotine and cotinine in women and their newborn infants. *JAMA* 1994: 271: 621–623.

Eliopoulos C., Klein J., and Koren G. Validation of self-reported smoking by analysis of hair for nicotine and cotinine. *Ther Drug Monit* 1996: 18 (5): 532–536.

Gerstenberg B., Schepers G., Voncken P., et al. Nicotine and cotinine accumulation in pigmented and unpigmented rat hair. *Drug Metab Dispos* 1995: 23: 143–148.

Glasgow R., Foster L., Lee M., et al. Developing a brief measure of smoking in the home: description and preliminary evaluation. *Addict Behav* 1998: 23: 567–571.

Gori G.B. Science, policy, and ethics: the case of environmental tobacco smoke. *J Clin Epidemiol* 1994: 47: 325–334.

Gori G.B. Environmental tobacco smoke and coronary heart syndromes: absence of an association. *Regul Toxicol Pharmacol* 1995: 21: 281–295.

Greenberg R.A., Bauman K.E., Glover L.H., et al. Ecology of passive smoking by young infants. *J Pediatr* 1989: 114: 774–780.

Haddow J.E., Knight G.J., Palomaki G.E., et al. Replacing creatinine measurement with specific gravity value to adjust urine cotinine concentration. *Clin Chem* 1994: 40: 562–564.

Hoffmann D., and Hoffmann I. Significance of exposure to sidestream tobacco smoke. *IARC Sci Publ* 1987: 81: 3–10.

Idle J.R. Titrating exposure to tobacco using cotinine — a minefield of misunderstandings. *J Clin Epidemiol* 1990: 43: 313–317.

Jaakkola M.S., and Jaakkola J.J. Assessment of exposure to environmental tobacco smoke. *Eur Respir J* 1997: 10: 2384–2397.

PM3006484812

Source: https://www.industrydocuments.ucsf.edu/docs/yzhj0001

Jarvis M.J., Russell M.A.H., Feyerabend C., et al. Passive exposure to tobacco smoke: saliva cotinine concentration in a representative population sample of non-smoking schoolchildren. *BMJ* 1985: 291: 927–929.

Jurado C., Kintz P., Menendez M., et al. Influence of the cosmetic treatment of hair on drug testing. *Int J Legal Med* 1997: 110 (3): 159–163.

Kintz P., Ludes B., and Mangin P. Evaluation of nicotine and cotinine in human hair. *J Forensic Sci* 1992: 37: 72–76.

Klein J., Forman R., Eliopoulos C., et al. A method for simultaneous measurement of cocaine and nicotine in neonatal hair. *Ther Drug Monit* 1994: 16: 67–71.

Knight J.M., Eliopoulos C., Klein J., et al. Passive smoking in children. Racial differences in systemic exposure to cotinine by hair and urine analysis. *Chest* 1996: 109: 446–450.

Koren G., Klein J., Forman R., Graham K., and Phan M.K. Biological markers of intrauterine exposure to cocaine and cigarette smoking. *Dev Pharmacol Ther* 1992: 18: 228–236.

Labrecque M., Marcoux S., Weber JP., et al. Feeding and urine cotinine values in babies whose mothers smoke. *Pediatrics* 1989: 83: 93–97.

Mizuno A., Uematsu T., Oshima A., et al. Analysis of nicotine content of hair for assessing individual cigarette smoking behavior. *Ther Drug Monit* 1993: 15 (2): 99–104.

Nafstad P., Botten G., Hagen J.A., et al. Comparison of three methods for estimating environmental tobacco smoke exposure among children aged between 12 and 36 months. *Int J Epidemiol* 1995: 24 (1): 88–94.

Nafstad P., Jaakkola J.J.K., Hagen J.A., et al. Hair nicotine concentrations in mothers and children in relation to parental smoking. *J Expos Anal Environ Epidemiol* 1997: 7 (2): 235–2339.

Nelson P.R. Submission to US Occupational Safety and Health administration hearing on the proposed standard on indoor air quality, Docket No. H-122, 1994.

Nilsen T., Zahlsen K., and Nilsen O.G. Uptake of nicotine in hair during controlled environmental air exposure to nicotine vapor: evidence for a major contribution of environmental nicotine to the overall nicotine found in hair from smokers and non-smokers. *Pharmacol Toxicol* 1994: 75: 136–1342.

Pichini S., Altieri I., Pellegrini M., et al. The analysis of nicotine in infants' hair for measuring exposure to environmental tobacco smoke. *Forensic Sci Int* 1997: 84: 253–258.

Strachan D.P., Jarvis M.J., and Feyerabend C. Passive smoking salivary cotinine concentrations, and middle ear effusion in 7-year-old children. *BMJ* 1989: 298: 1549–52.

Uematsu T., Mizuno A., Nagashima S., et al. The axial distribution of nicotine content along hair shafts as an indicator of changes in smoking behaviour: evaluation in a smoking cessation programme with or without the aid of nicotine chewing gum. *Br J Clin Pharmacol* 1995: 39: 665–669.

U.S. Environmental Protection Agency (U.S. EPA). Respiratory health effects of passive smoking: lung cancer and other disorders. Report of the U.S. Environmental Protection Agency, Vol. 4. Washington, DC, EPA/600/6-90/006F, Monograph, 1992, pp. 36–37.

Wagenknecht L.E., Burke G.L., Perkins L.L., et al. Misclassification of smoking status in the CARDIA study: a comparison of self-report with serum cotinine levels. *Am J Public Health* 1992: 82: 33–36.

Wang X., Tager I.B., Van Vunakis H., et al. Maternal smoking during pregnancy, urine cotinine concentrations, and birth outcomes. A prospective cohort study. *Int J Epidemiol* 1997: 26: 978–988.

Zahlsen K., and Nilsen O.G. Nicotine in hair of smokers and non-smokers: sampling procedure and gas chromatographic/mass spectrometric analysis. *Pharmacol Toxicol* 1994: 75: 143–149.

Zahlsen K., Nilsen T., and Nilsen O.G. Interindividual differences in hair uptake of air nicotine and significance of cigarette counting for estimation of environmental tobacco smoke exposure. *Pharmacol Toxicol* 1996: 79: 183–190.

Zatarian V.G., Ott W.R., and Duan N. A quantitative definition of exposure and related concepts. *J Expos Anal Environ Epidemiol* 1997: 7: 411–437.

PM3006484813

Source: https://www.industrydocuments.ucsf.edu/docs/yzhj0001